

## REMARKS

Claims 1-14 are pending and under examination. Claims 1-14 have been canceled. New claims 15-35 have been added. Support for the new claims can be found throughout the specification and the claims as filed. In particular, support for new claims 15-35 can be found in original claims 1-14 and, for example, on page 4, lines 2-5. Support for the recitation in claims 19-21, 26 and 33 of the term "pharmaceutical composition" can be found, for example, on page 6, lines 12-15, which describes formulating pharmaceutical compositions or carriers. Support for new claims 16, 23 and 30 reciting coding sequences under the control of a single promoter can be found, for example, on page 6, lines 1-2. Support for the amendment to the specification on page 7 can be found in original claim 14. Accordingly, these amendments and new claims do not raise an issue of new matter and entry thereof is respectfully requested.

Without addressing the merits of the rejections set forth in the Office Action mailed July 28, 2005, Applicants have canceled claims 1-14 without prejudice to Applicants pursuing these claims in a related application.

### Objection to the Specification

The objection to the specification is respectfully traversed. The specification has been amended as requested by the Examiner to provide antecedent basis for terms recited in original claim 14. Accordingly, Applicants respectfully request that this objection be withdrawn.

### Objections to the Claims

The objection to claims 2, 4-6, 8, 11 and 14 for various informalities is respectfully traversed. The objection to these claims has been rendered moot by the cancellation of these claims. Furthermore, the informalities have been corrected in the new claims. Accordingly, Applicants respectfully request that this objection be withdrawn.

### Rejection Under 35 U.S.C. § 112, First Paragraph

The rejection of claims 1-14 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description is respectfully traversed. Applicants submit that this rejection has been

rendered moot by the cancellation of claims 1-14. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 102

The rejection of claims 1-12 and 14 under 35 U.S.C. § 102(e) as allegedly anticipated by Depinho, U.S. publication 2002/0193325, is respectfully traversed. Applicants submit that this rejection has been rendered moot by the cancellation of claims 1-12 and 14. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Rejection Under 35 U.S.C. § 103

The rejection of claims 1-14 under 35 U.S.C. § 103 as allegedly obvious over Roth et al., U.S. Patent No. 5,747,469, in view of Lu et al., Cancer Res. 62:1305-1310 (2002), and/or Tango et al., Hum. Gene Ther. 13:1373-1382 (2002), and further in view of Almond et al., WO 99/47690, is respectfully traversed. Applicants submit that this rejection has been rendered moot by the cancellation of claims 1-14. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Regarding new claims 15-35, Applicants respectfully submit that these claims are unobvious over Roth et al., alone or in combination with Lu et al. and/or Tango et al. and/or Almond et al. Applicants respectfully submit that, based on the teachings in these references, one skilled in the art would have had no reasonable expectation of success for the unexpected properties of the claimed bicistronic construct containing p53 and p14ARF and methods using the bicistronic construct. In particular, the specification teaches that the bicistronic construct containing p53 and p14ARF was found to achieve complete suppression of tumor growth and viability at doses 20 times lower than doses needed to achieve suppression with single gene vectors for p53 and p14ARF (page 8, lines 6-10). Furthermore, the bicistronic vector exhibited the unexpected property of being more effective than a combination of the two single gene vectors provided at an equivalent dose for p53 or ARF (page 8, lines 10-12). Moreover, the viability of several tumor cell lines of different origins was abolished using very low vector to cell ratios (page 8, lines 21-22). In addition, the bicistronic vector was able to slow tumor growth at a dose that required chemotherapy when the same dose was used with a vector

containing p53 alone (page 9, lines 1-16). Thus, it is respectfully submitted that one skilled in the art would have had no reasonable expectation of the unexpected properties of the claimed bicistronic vector containing p53 and p14ARF and methods of using the bicistronic vector. Accordingly, Applicants respectfully submit that the claimed compositions and methods are unobvious over Roth et al., alone or in combination with Lu et al. and/or Tango et al. and/or Almond et al.

Double Patenting

The Office Action has indicated that claims 4 and 5 are considered to be substantial duplicates of claims 2 and 3. In light of the cancellation of claims 2-5 and addition of new claims 15-35, Applicants believe that this issue has been rendered moot.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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